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Room: Room 1.40

Standards in prophylaxis: Prevention of invasive aspergillosis in patients with hematologic malignancies

D. Kontoyiannis

University of Texas, Houston, USA

Best practice strategies regarding primary antifungal prophylaxis in leukemia patients and in hematopoietic stem cell transplant recipients continue to evolve. For this prophylaxis to be beneficial and cost-effective, the risk of a life-threatening invasive fungal infection (IFI) should outweigh the risks of toxic effects and drug interactions introduced by the antifungal agent used. Furthermore, the improved survival of such patients with IFIs creates pressing issues regarding optimization of secondary antifungal prophylaxis. Not all patients with hematologic cancer recipients have the same risk of IFIs. Well tolerated and pharmacokinetically reliable, broad-spectrum antifungals, especially azoles, have the potential for reducing IFI-associated mortality in these patients. Further refinement of risk stratification and risk/benefit analysis (including pharmacoeconomic analysis) is needed. Stratification of IFI risk could be further sharpened based on emerging genetic, metabolic risk factors. Despite robust data from randomized prospective studies, personalized decisions and reliance on institution-specific epidemiologic data are still expected to be a major part of "art and science" of prophylaxis for fungal infections in severely immunosuppressed hosts.

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Implication of current resistance trends on community-acquired respiratory tract infection (CA-RTI) management

A. Brink

Milpark Hospital, Johannesburg, South Africa

As the prevalence of antibiotic-resistant *Streptococcus pneumoniae*, including multidrug-resistant strains is variable world-wide[1], first-line therapy with beta-lactams, macrolides, and increasingly quinolones, in some regions has become limited in the treatment of respiratory tract infections (RTIs). Therefore, one of the important principles for appropriate antibiotic prescribing and effective outcomes in this clinical setting is to recognise local resistance prevalence.[2] The aim of surveillance is both to guide empirical In addition, introduction of pneumococcal vaccines may alter the predominant serotypes with potentially unique antimicrobial susceptibility patterns.

There have been a number of international surveillance systems established including the ALEXANDER PROJECT, PROTEKT, LIBRA, SENTRY, ANSORP[4] and SIREVA.[5] Survey Of Antibiotic Resistance (SOAR)[6] is the latest of the international surveillance studies that offer standardised, internationally recognised methods that provide quantitative data (minimum inhibitory concentrations [MIC]) that may show slight shifts in resistance - as seen in published SOAR data.[6] These 'shifts' in antibiotic MICs can be overcome by extending the time above MIC (T > MIC) for which amoxicillin, for example, is present in serum.[7]

In addition to MIC shifts, an increase in the prevalence of *Haemophilus influenzae* has been observed in upper RTIs subsequent to wide-scale use of pneumococcal conjugate vaccines in children.[8] This phenomenon, as well as an increase in beta-lactamase production amongst *H.influenzae* in certain parts of the world, has necessitated the first line empirical use of amoxiciilin-clavulanate as opposed to amoxicillin alone.[9] Continuous surveillance through standardised systems is therefore crucial to guide clinicians in rational antibiotic prescribing for community acquired RTIs.

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What is 'judicious use of antibiotics' and is it achievable in children?

R. Dagan

Ben-Gurion University and Soroka University Medical Center, Beer-Sheva, Israel

Judicious use of antibiotics is promoted largely because of the threat of antibiotic-resistant pathogens. The most common reasons for antibiotic prescriptions in all ages are respiratory tract infections (RTIs). The most common patients to receive antibiotics are infants and young children, and among these, the commonest diagnosis for which antibiotics are prescribed is otitis media. Antibiotic resistance in the community is spread through selection of antibiotic-resistant respiratory flora submitted to antibiotic pressure during treatment of various acute diseases. Not all antibiotics are equal in their effect on promotion of antibiotic resistant organisms. Using the pneumococcus paradigm, azithromycin is the antibiotic with the highest promotion of resistance, due to its long half life and low extra-cellular concentration; followed by oral cephalosporins. Traditionally, "judicious use of antibiotics" is translated by most clinicians as "reducing antibiotic use". However judicious use means much more than that. There is a need to consider all the following to successfully execute a judicious use of antibiotics (as summarized by Ball *et al*, *Journal of Antimicrobial Chemotherapy* 2002;49:31-40): 1) Treatment of bacterial infections only; 2) optimize treatment by diagnosis and severity assessment; 3) maximize bacterial eradication; 4) recognize local resistance prevalence; 5) utilize pharmacokinetics/pharmacodynamics for